

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE  
in its capacity as elected Office

Date of mailing (day/month/year)  
04 July 2001 (04.07.01)

International application No.  
PCT/US00/22801

Applicant's or agent's file reference  
18484-23-1PC

International filing date (day/month/year)  
18 August 2000 (18.08.00)

Priority date (day/month/year)  
20 August 1999 (20.08.99)

## Applicant

GHIVIZZANI, Steven, C. et al

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
19 March 2001 (19.03.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Charlotte ENGER

Telephone No.: (41-22) 338.83.38

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 484-23-IPC	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. T/US00/22801	International filing date (day/month/year) 18 AUGUST 2000	Priority date (day/month/year) 20 AUGUST 1999
International Patent Classification (IPC) or national classification and IPC base See Supplemental Sheet.		
Applicant UNIVERSITY OF PITTSBURGH OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets.
- ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 9 MARCH 2001	Date of completion of this report <input checked="" type="checkbox"/> the description, page 14 MAY 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer <div style="text-align: center;"> <b>TERRY J. DEY</b>  <b>PARALEGAL SPECIALIST</b>  <b>TECHNOLOGY CENTER 1600</b> </div>

**Basis of the report**

With regard to the elements of the international application:\*

- ☒ the international application as originally filed
- ☒ the description:  
pages 1-32 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_
- ☒ the claims:  
pages 33-35 , as originally filed  
pages NONE , as amended (together with any statement) under Article 19  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_
- ☒ the drawings:  
pages 1-5 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_
- ☒ the sequence listing part of the description:  
pages NONE , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
- ☒ The amendments have resulted in the cancellation of:  
☒ the description, pages NONE  
☒ the claims, Nos. NONE  
☒ the drawings, sheets/fig NONE

☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16*

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

statement

Novelty (N)	Claims	<u>1-32</u>	YES
	Claims	<u>NONE</u>	NO
Inventive Step (IS)	Claims	<u>1-32</u>	YES
	Claims	<u>NONE</u>	NO
Industrial Applicability (IA)	Claims	<u>1-32</u>	YES
	Claims	<u>NONE</u>	NO

citations and explanations (Rule 70.7)

Claims 1-32 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the claimed methods for providing a heterologous protein, heterologous growth factors and/or compositions for expression of a heterologous gene in a subchondral cell in a joint of a mammal.

----- NEW CITATIONS -----

NONE

Supplemental Box

to be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:

C(7): A61K 48/00; C12N 15/00, 15/85, 15/90; C07H 21/04 and US Cl.: 514/44; 435/440, 455; 536/23.1

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PCT

NOTIFICATION OF TRANSMITTAL OF  
INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing (day/month/year)		29 AUG 2001
Applicant's or agent's file reference 18484-23-IPC		IMPORTANT NOTIFICATION
International application No. PCT/US00/22801	International filing date (day/month/year) 18 AUGUST 2000	Priority Date (day/month/year) 20 AUGUST 1999
Applicant UNIVERSITY OF PITTSBURGH OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION		

- The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
- A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
- Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Authorized officer

GERALD G. LEFFERS JR.

TERRY J. DEY  
PARALEGAL SPECIALIST

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT US00-22801

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>		
IPC(7) : A61K 48 00; C12N 15 00; 15 85; 15 90; C07H 21 04 US CL : 514-44; 435-440; 455; 536-23.1		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols) U.S. : 514-44; 435-440; 455; 536-23.1		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Extra Sheet.		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
A	SONG et al. "Plasmid DNA encoding transforming Growth Factor-B1 supresses chronic disease in a Streptococcal cell wall-induced arthritis model," The Journal of Clinical Investigation, June 1998, Vol. 101, No. 12, pages 2615-2621, see entire document.	1-32
A	GHIVIZZANI et al. "Direct adenovirus-mediated gene transfer of interleukin 1 and tumor necrosis factor alpha soluble receptors to rabbit knees with experimental arthritis has local and distal anti-arthritic effects. Proceedings of the National Academy of Sciences," USA, April 1998, Vol. 95, pages 4613-4618, see entire document.	1-32
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents	* T	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
* A document defining the general state of the art which is not considered to be of particular relevance	* X	document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
* E earlier document published on or after the international filing date	* Y	document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
* L document which may throw doubts on priority claims or which is cited to establish the publication date of another citation or other special reason (as specified)	* X	document member of the same patent family
* O document referring to an oral disclosure, use, exhibition or other means		
* P document published prior to the international filing date but later than the priority date claimed		
Date of the actual completion of the international search 28 SEPTEMBER 2000		Date of mailing of the international search report 25 OCT 2000
Name and mailing address of the ISA US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230		Authorized officer my initials GERALD G. LEFFERS JR Telephone No. (703) 308-0196

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## INTERNATIONAL SEARCH REPORT

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## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,766,585 A (EVANS et al) 16 June 1998 (16.06.98), see entire document, especially columns 1-5.	1-32
A	US 5,770,580 A (LEDLEY et al) 23 June 1998 (23.06.98), column 21, lines 35-57.	1-32
A	WO 92/11359 A1 (GLORIOSO et al.) 09 July 1992 (09.07.92), see entire document.	1-32
A,P	US 6,077,987 A (BREITBART et al) 20 June 2000 (20.06.00), columns 6-8.	1-32



# INTERNATIONAL SEARCH REPORT

International application No.

PCT US00/22801

## B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

EAST: JPO, EPO, DERWENT, USPAT STN: MEDLINE, EMBASE, BIOSIS, CAPLUS  
search terms: inventors' names, subchondral bone or cell, cartilage, chondrocyte, chondrogenic, TGF-1, IGF-1, cytokine  
or cytokine inhibitor, gene transfer or therapy, perforation, abrasion, cationic lipid, microfracture

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